

PDGF enhances store-operated Ca²⁺ entry by upregulating STIM1/Orai1 via activation of Akt/mTOR in human pulmonary arterial smooth muscle cells.

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Public Summary:

Platelet-derived growth factor (PDGF) and its receptor are known to be substantially elevated in lung tissues and pulmonary arterial smooth muscle cells (PASMC) isolated from patients and animals with pulmonary arterial hypertension. PDGF has been shown to phosphorylate and activate Akt and mTOR in PASMC. In this study, we investigated the role of PDGF-mediated activation of Akt signaling in the regulation of cytosolic Ca(2+) concentration ([Ca(2+)](cyt)) and cell proliferation. PDGF activated the Akt/mTOR pathway and, subsequently, enhanced store-operated Ca(2+) entry (SOCE) and cell proliferation in human PASMC. Inhibition of Akt attenuated both the increase in [Ca(2+)](cyt) due to SOCE and PASMC proliferation. This effect correlated with a significant downregulation of STIM and Orai, proposed molecular correlates for SOCE in many cell types. The data from this study present a novel pathway for the regulation of Ca(2+) signaling and PASMC proliferation involving activation of Akt in response to upregulated expression of PDGF. Targeting this pathway, may lead to development of a novel therapeutic option for the treatment of pulmonary arterial hypertension.

Scientific Abstract:

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